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Compensatory cerebral motor control following presumed perinatal ischemic stroke

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ABSTRACT

A fifteen year-old left-handed girl presented with right-sided focal motor seizures. Neuroimaging showed a large left hemisphere lesion compatible with a middle cerebral artery stroke of presumed perinatal origin. She was not previously diagnosed with a motor deficit, although neurological examination now revealed that it required more attention to use the affected right hand during both unimanual and bimanual movements. As perinatal stroke provides unique insight in plasticity of the brain, we performed functional and diffusion brain imaging showing reduction of pyramidal efferents from the affected hemisphere and extensive compensatory bilateral brain activations during right hand movements. The activated compensatory network was extensive, comprising regions involved in higher-order motor control and visuospatial attention, now recruited during simple right unimanual and bimanual antiphase movements. This pre-existing network for simple movements that healthy subjects only need to recruit for more complex motor actions, enabled our patient to perform simple right-handed movements.

INTRODUCTION

Perinatal ischemic stroke may be asymptomatic in the early phase despite its acute onset. Most of such lesions become symptomatic within the first year.[1] Despite uncertainties about its cause and exact timing, perinatal stroke provides unique insight in the plasticity of the brain. In this case report, we describe a girl with a presumed ischemic perinatal stroke in the territory of the left middle cerebral artery distal to the lenticulostriate arteries.[2,3] She came under medical attention at the age of fifteen years with focal seizures as first clinical manifestation. We used functional and diffusion brain imaging to identify compensatory networks for motor control that allowed the event to remain unnoticed as a medical problem for many years despite the large cortical defect.

CASE STUDY

Our fifteen year-old female patient had initially been admitted to another hospital because of right-sided focal motor seizures. CT revealed a large left hemisphere defect (fig. 1A). Seizures persisted despite antiepileptic drug treatment and she was therefore referred to our hospital. She appeared to be extremely left-handed and clumsy on the right side since childhood. Neurological examination revealed mild pyramidal features on the right side including impaired finger tapping and hand opening and closing, as well as minimally reduced muscle strength on the right side. Alternating flexor-extension finger movements made by the two hands in antiphase were less accurate and required enhanced concentration. MRI of the brain confirmed a large defect in the middle cerebral artery territory (fig.1B). The history of the patient revealed no complications during pregnancy or delivery and no symptomatic periods during infancy. During standardized checks at young age her psychomotor development had been considered within normal limits. These characteristics from the general assessment of her developmental history, together with the large defect in de territory of the middle cerebral artery and the minor neurological symptoms found at later age, are consistent with a presumed perinatal ischemic stroke[2], an entity that is known to be able to produce very subtle symptomatology.[1]

METHODS

We performed fMRI to localize brain regions involved in right and left unimanual as well as bimanual inphase and antiphase hand opening and closing, cued by one Hertz beeps. The balanced randomized conditions were presented in two blocks during acquisition of gradient-echo T2* blood oxygen level dependent (BOLD) in a 3 Tesla scanner. In between the two blocks a T1 anatomical scan was performed. Using statistical parametric mapping version 8 (www.fil.ion.ucl.ac.uk/spm), unimanual right and left hand movements were compared with each other. Similarly, bimanual inphase and antiphase movements were also compared with each other. A separate session was performed to acquire DTI images with 60 directions with a *b*-value of 1000 s/mm^2 followed by a *b*0 image. Another T1 reference scan was acquired in the second session. Probabilistic analysis of DTI images was performed with FMRIB Software Library (FSL) version 4.1.9 (www.fmrib.ox.ac.uk/fsl). Further details of the methods are provided in the web only supplement.

RESULTS

Tractography of the right and left pyramidal tracts showed a smaller and more anteriorly positioned pyramidal tract in the affected left hemisphere (fig.1C). Comparison of left with right hand movements showed focal activations of the pre- and postcentral gyrus of the contralateral right hemisphere and ipsilateral left cerebellum (fig.1D). Comparison of movements of the affected right hand with those of the left hand, however, showed significant activation of an extensive bilateral network comprising the contralateral left pre- and postcentral gyrus, bilateral pre-supplementary motor area, anterior and middle cingulate cortex, right superior parietal lobule, bilateral dorsolateral frontal regions, bilateral superior temporal, right insula, right striatum and bilateral cerebellar activation dominant on the right side, i.e., opposite to the extensive pattern of activations in the left hemisphere (fig.1E).

Comparison of inphase with antiphase movements revealed no significant clusters of increased activation, while antiphase movements showed a pattern of increased activations compared to inphase movements, comprising bilateral dorsal premotor cortex, right supplementary motor area (SMA), bilateral insula, right occipito-temporal junction and bilateral cerebellum (fig.1F).

DISCUSSION

We demonstrated that the large presumably perinatal defect in the left hemisphere of our patient resulted in reduced pyramidal efferents from the affected hemisphere and extensive compensatory bilateral brain activations during right hand movements. Simple unimanual movements of the hand typically reveal a delineated pattern of activations restricted to the contralateral sensorimotor cortex and ipsilateral cerebellum, also in left handed subjects.[4] During simple movements with the non-dominant hand, activation of these core elements of a motor network may be slightly stronger but remains still concise, both in right- and left-handed healthy subjects.[5] Our patient, however, demonstrated a widespread network of activations related to performing just simple unimanual movements with the non-dominant right hand. This was similarly shown during bimanual antiphase movements. This extensive pattern represents a (task-related) motor network, but is also implicated in spatial attention as inferred from activations of the dorsolateral frontal regions in conjunction with superior parietal lobule and superior temporal regions. The latter point at an increased attentional demand, especially with respect to (visuo)spatial characteristics of movements. This corresponds with the clinical characteristics of our patient, who was able to perform the movements, but reported that movements with the affected right hand or bimanual antiphase movements indeed required more attention. Her natural preference of looking at the affected hand during movements, which was not possible during the fMRI experiment, may underscore a stronger contribution of (visuo)spatial attention. The extensive motor and spatial attention networks may be easily recruited in healthy subjects as demonstrated by its identification during resting state.[6] Its widespread task-related activation in healthy subjects particularly occurs during more complex movements, also in left-handed subjects,[4] and during motor learning.[7] Apparently, this pre-existing network, used for complex motor action in healthy subjects, is recruited for simple movements in our patient to compensate the large hemisphere defect. In this respect, plasticity points at differential changes in existing networks, more than a fully new 'rewiring' of the brain.

In conclusion, during right unimanual and bimanual antiphase movements, our patient with a perinatal unilateral ischemic stroke showed compensatory activation of an extensive network comprising brain regions related to motor functions and visuospatial attention, which enabled her to perform these movements reasonably well. She thus appeared to use a pre-existing network for simple movements which healthy subjects only need to recruit for more complex motor tasks.

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COMPETING INTEREST

No conflict of interests.

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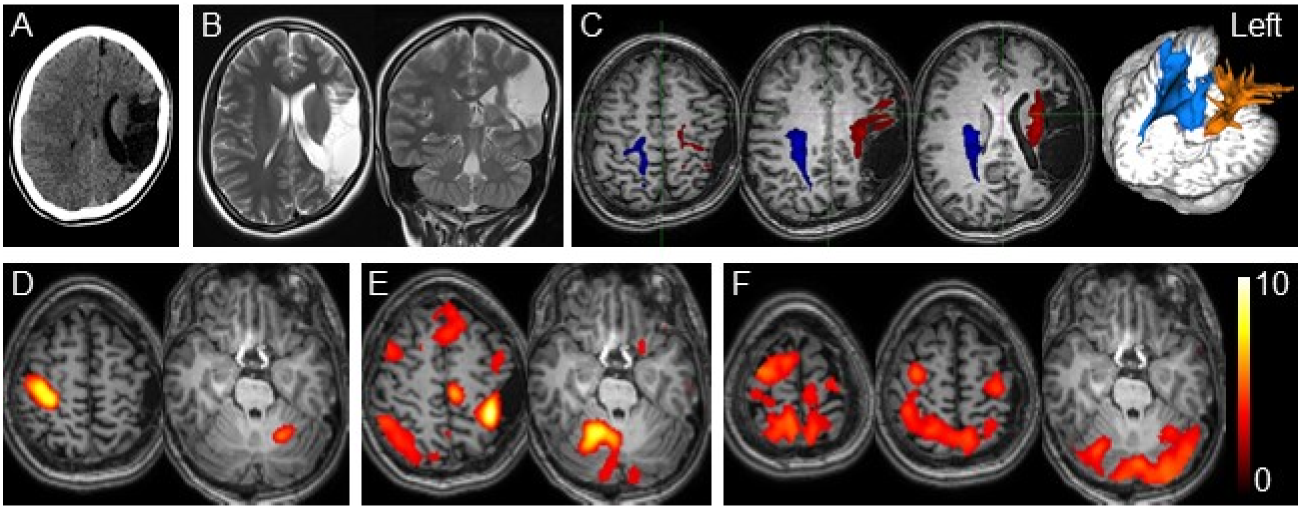
FIGURE 1 – Anatomical and functional images



Anatomical and functional images of the patient's brain. The CT scan (A) en T2 weighted MRI scan (B) depict the left hemisphere defect compatible with an ischemic stroke in the distal MCA territory sparing the basal ganglia. MRI sections are in transverse (left) and coronal (right) orientation. Probabilistic tractography results (C) display the connections of the pyramidal tract for the left (orange/red) and right (blue) cerebral peduncle. DTI image display range was set at 500-5000 hits. Functional MRI scans (D-F) show activations during successively contrasting opening and closing movement of the hands; left versus right (D), right versus left (E) and antiphase versus inphase movements (F). Functional MRI images are thresholded at p=0.001 uncorrected with a voxel extent of eight voxels. T-values for functional images are displayed in the colour bar.